DETAILED ACTION

Applicant's filing of the RCE and amendment to add new claim 15 are acknowledged.

The Examiner and Applicant's Representative held an interview on 9/22/09, the substance of which is included herein:

> *An interview was scheduled to discuss "spherical microcapsule" arrangement of the known compound, following the filing of the RCE. Applicant has argued of record it was unexpected to take the linear form and convert it into the spherical form and into a microcapsule, based on the findings after synthesizing. The Examiner indicated that taking linear molecules and converting to spherical form, even with the process applied, is well known in the art, even if not previously applied to this specific compound. As is putting compounds into microcapsules. Thus, the question remains as to whether Applicants findings can really be given weight as 'unexpected'. The Examiner indicated a First Action on the Merits will be forthcoming after the RCE so that Applicant may have sufficient time to present evidence/arguments that this linear to spherical form would have been unexpected/unpredictable to one of ordinary skill in the art, as well as putting into microcapsule administration form.*

Thus, in line with the above analysis conveyed by interview, the present Office Action maintains the 35 USC 103 rejection in its entirety. But is sent as a Non-Final, in order to afford Applicant ample time to address the rejection/disposition by argument, amendment or other evidence (e.g. 1.132 Declaration).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim 14 and new claim 15 are rejected under 35 U.S.C. 102(b) as being anticipated by either Kogiso et al. (US 6,136,956, issued 10/24/00, two inventors in common with the present application) or Agency of Ind. Science & Techn. (now JP-B-3012932 Patent, 12/17/99, application JP 11-322787, cited in IDS of 4/4/05) - both discussed collectively under Kogiso et al. in view of Tsilosani et al. (US 6,743,638), is maintained for the reasons of record. Applicant's arguments have been considered but are not found persuasive.

Applicant argues one of ordinary skill in the art would not have been motivated to arrive at, nor found predictable, the present invention based on the combination of Applicant's own earlier work (Kogiso et al.) in view of Tsilosani et al. Applicant relies upon:

> Liposome can be easily obtained by treating a suspension of a phospholipid. The production process thereof has been reported by Bangham *et al.* in the following reference documents:

A.D.Bangham and R.M.C. Dawson, Nature (1958) 182, 1292-1293

A.D. Bangham, Nature (1961) 192, 1197-1198

A.D. Bangham and R.W. Horne, Nature (1962) 196, 952-953.

However, none of these references or relevant passages thereof have been included in the response, such that the Examiner can fully consider these references as relevant to Applicant's arguments. Applicant goes on to indicate that Israelachavili et al. shows a 'correlation' between forms of packing molecules and the structures formed therefrom. The Examiner asserts this structure variables (e.g. truncated cone) based on various packing means, were known or predictable in the art at the time of the invention. But even if not, such a 'cone' structure is not claimed and this argument finds little application to the invention as claimed. Rather, the issue is whether this known compound (PRODUCT) could have been into a spherical microcapsule (PRODUCT) or any other PRODUCT, known at the time of the invention? The answer is yes. A product comprising a known product is still that product. Applicant's arguments are directed to methods of making products (e.g. truncated cone) via packing methodology – which bear no weight on the patentability of another product comprising a known product.

The rejection is repeated below for continuity of record:

The rejection is virtually identical, other than the recitation of Tsilosani et al.

It is noted that Applicant's earliest effective priority date is 10/7/02, greater than one year after the '956 patent issued.

Kogiso et al. teach:

1) the identical compound of formula I (entire document). As the present specification page 1-2 recites: "[i]t is described, for example, in Japanese Patent No. 3012932 and Chem. Comm., 1998, pp. 1791-1792 that the above compound forms a nano-scale fiber having a width of about 10 to 30 nm when an aqueous alkaline solution of the compound is gradually acidified"]. Kogiso et al. ;

2) linear products, namely fibers and fibrous assemblies, comprising the same; as well as spherical products, the easier to make product as discussed (col. 1, lines 21-34); and

3) a method of making the same using a substrate having hydrophilicity (e.g. glass vial), alkali metal salt, precipitated under a weakly acid atmosphere (Example 1 ; col. 2, lines 21-31; claims 5-7).

Specifically, the background on the art's processing of the easier made fine spherical versions of the '956 patented fibers/fibrous assemblies of Kogiso et al. is described in Kogiso et al. at col. 1, lines 21-34 and col. 3, lines 29-53:

"... well known, fibrous assemblies of a peptide lipid are widely employed in many applications, besides the applications as a drug delivery system or an adsorbent, in the fields of. medical and pharmaceutical sciences as a bioadaptable material, in the fields of electronic and information-processing technologies as a material of microelectronic parts, in the fields of food industries, agriculture, forestry and fiber industries as an emulsifying agent, stabilizer, dispersing agent or moisturizing agent and so on.

In the prior art, spherical assemblies obtained from a natural phospholipid or so-called liposomes are known among molecular aggregates formed from a phospholipid. Such a spherical assembly is usually prepared by the thin-film method, thermal dispersion method, cholic acid method or reversed-layer evaporation method (see, for example, "Seitaimaku Jikkenhou" (Experimental Methods for Biomembra.nes), volume 2, page 185, published by Kyoritu Shuppan Co.).

Each of these prior art methods, however, requires extremely high skillfulness. In addition, the *molecular aggregates* obtained by these methods are limited to a *monolayered vesicle* or *spherical multilayered vesicle* and long fibrous assemblies cannot be prepared thereby. On the other hand, several method are disclosed, for example, in Journal of the American Chemical Society, volume 119, pages 9120-9124 (1997) for the preparation of a fibrous assembly from a synthetic amphiphilic compound in water. Each of these methods, however, is a method in which fibrous assemblies are obtained by spontaneous *precipitation* or crystallization from a hot concentrated *aqueous solution* containing an *amphiphilic compound* so that the yield of the product is necessarily limited.

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The various reagents, i.e. amino group-protective agent, carboxyl group-protective agent and coupling agent, and the procedures in the above described reaction can be conventional and freely selected from those used in the prior art for peptide synthesis. The intermediate peptide compounds formed in the course of the reaction can readily be isolated and purified by washing

the reaction mixture with an acid or alkali aqueous solution followed by recrystallization or reprecipitation.

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The fine fibrous assembly of the invention is obtained from an aqueous solution of an alkali metal salt of the above described bola-form peptide lipid compound by causing precipitation thereof in a crystalline form.

The only thing Kogiso et al. does not expressly teach is that said fine spherical products have "uniform molecular orientation" or the word "microcapsule" (and that said microcapsule can encompass a substance having hydrophilicity, e.g. glass?). Hence the present rejection is made under 103, rather than 102, as expressly anticipated.

Tsilosani et al. teach nanoparticles/microcapsules/spherical liposomes of varying size, wherien "In the embodiment of FIG. 1, a particulate containment means such as a liposome (1) contains signal generating agents (2) which generate signal in
response to the presence of an ion such as H.sup.+. Suitable agents (2) are
therefore pyranine" (see Fig. 1).

It would have been obvious to one of ordinary skill in the art at the time of the invention to have made a "uniformly oriented" and/**or "microcapsule" spherical version, in linear or cyclical form**, comprising pyranine as the visible agent therein, of the fiber/fibrous assemblies comprising compounds of Formula 1 in Kogiso et al., because Applicant's earlier work expressly states that making the spherical versions of such constructs is easier and known and the

advantageous teachings of Tsilosani et al. indicate that spherical bodies of minute proportion comprising pyramine were known in this same art. And as previously stated, it was the linear, fiber versions that posed enablement & development issues, not spherical constructs, which were well known in the art to have uniform molecular orientation and be used in the biomedical fields as microcapsules, which encapsulate water-attracted compounds/molecules. Thus, even though a secondary reference to the same need not have been necessary or further expounding necessary, as evident by the recited specification pages above, from Kogiso et al., such has not been provided to clarify the record.

Additionally, and added here, as noted in the interview summary: *taking linear molecules and converting to spherical form, even with the process applied, is well known in the art, even if not previously applied to this specific compound. As is putting compounds into microcapsules.*

Thus, from the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MAURY AUDET whose telephone number is (571)272-0960. The examiner can normally be reached on M-Th. 7AM-5:30PM (10 Hrs.).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MA, 10/25/2009

/Maury Audet/
Examiner, Art Unit 1654
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